REMARKS

Claims 15, 18-29, 63, 65, and 66 are pending in the Application. In the Office Communication mailed on November 13, 2009, the Examiner maintains certain rejections and raises several new rejections. For clarity, the rejections are listed below in the order in which they are addressed herein.

I. Claims 15, 18-21, 23-25, 28-29 and 63-66 stand rejected under 35 U.S.C. 102 (b) as allegedly being anticipated by Egner et al (Chern. Commun., 1997);

II. Claims 15-16, 18-19, 22-25, 28-29 and 63 stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Yamashita et al (WO 95/32425) (as evidenced by Tao Jia-ping et al(Chinese Journal of Physical Medicine (Vol. 17(3), September 1995, P 168-171);

III. Claims 15 and 18-21 stand rejected under 35 U.S.C. 102(e) as allegedly being anticipated by Seul et al (USP 7083914);

IV. Claims 15, 18-29, 63 and 65-66 stand rejected under 35 U.S.C. 102(e) as allegedly being anticipated by Kauvar et al (USP 6642062) (as evidenced by Tao Jia-ping et al(Chinese Journal of Physical Medicine (Vol. 17(3), September 1995, p 168-171) and by applicants' disclosure of known prior art.;

V. Claims 15, 18-29, 63 and 65-66 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over anyone of the cited references above e.g., Egner et al, Kauvar, Yamashita or Seul (hereinafter the primary references) in view of either Kris et al (USP 6238869) or Kimura et al (USP 6228480);

The Claims Are Not Anticipated

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. MPEP 2131, citing *Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d. 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).*

I. Claims 15, 18-21, 23-25, 28-29 and 63-66 stand rejected under 35 U.S.C. 102 (b) as allegedly being anticipated by Egner et al (Chern. Commun., 1997). As discussed in the Amendment and Response filed on July 13, 2009 and incorporated here, Claim 15 recites that each carrier in the plurality of distinctively identifiable carriers comprises at least two light

emanating features comprising a light scattering feature and a molecular fluorescence feature. Applicants pointed out that the beads of Egner do not comprise both a light scattering feature and a molecular fluorescence feature.

Response to Arguments

The Examiner points to Egner at page 735, paragraph bridging col. 1 and col. 2:

> "Labeling down . . . . the limits were determined by the amount of background fluorescence and Raman scattering from the bead."

(Office communication, page 4)

Based on the passage above, the Examiner points to the Raman scattering mentioned by Egner and asserts that Egner discloses a "light scattering feature" in accordance with the instant claims (Office communication page 4). Applicants respectfully disagree. The mere fact that there is Raman scattering from a bead of Egner is not indicative that Egner discloses a bead having a "light scattering feature" as recited in the instant claims. The "light scattering feature" of the instant claims must, in combination with at least one other feature, define the corresponding distinctive code for its respective carrier. See, *e.g.*, Claim 15, reciting " wherein individual carriers comprise all the **features that define a corresponding code.**" An attribute of a bead that is the same for all beads in a mixture, or that does not provide any distinction between any beads in a mixture, cannot contribute to defining a distinctive code for a bead within the mixture. Such an attribute may be an aspect of the bead, but it is not a "feature" as recited in the instant claims.

The Examiner has pointed to a general statement about Raman scattering from a bead defining the lower limit of detection of the fluorescent dye used to label the beads of Egner. Enger does not, however, teach that the Raman scattering observed was or could be used in combination with molecular fluorescence as a second "feature" defining a distinctive code. In fact, Egner does not teach or even suggest that Raman scattering provides any useful means of distinguishing one bead from another. As such, the Raman scattering disclosed by Egner does not have the properties required by the "light scattering feature" of the claims. Applicants therefore maintain that Egner fails to teach each of the elements of the instant claims, and as

such, Claims 15, 18-21, 23-25, 28-29 and 63-66 are not anticipated by Egner. Applicants respectfully request that these rejections be withdrawn.

II. Claims 15-16, 18-19, 22-25, 28-29 and 63 stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Yamashita et al (WO 95/32425, hereafter referred to as "Yamashita"), as evidenced by Tao Jia-ping et al(Chinese Journal of Physical Medicine (Vol. 17(3), September 1995, P 168-171) and by applicants' disclosure of known prior art. In particular, the Examiner has drawn attention to the passage of Yamashita beginning at page 17, line 12 *et seq*. and asserts that the Yamashita disclosure inherently contains the features of light scattering and fluorescence. Applicants respectfully disagree with this allegation.

First, the Examiner has provided no evidence that the beads of Yamashita have as an intrinsic attribute a light scattering feature that is distinct between the different particles such that the light scattering attribute serves to define a distinctive code for its respective bead. As discussed above, the "features" of the instant claims are recited as defining a distinctive code for a bead within the mixture.

The cited passage of Yamashita discloses the preparation of combinatorial libraries, which are synthesized on beads that are separated into pools or groups, wherein the beads within each group are similarly tagged and wherein each group is uniquely tagged (see page 5, lines 12 to 18). The term "*tag*" is defined on page 4 as "an encoding characteristic of a bead or group of beads which is capable of being sorted by flow cytometry, such as differences in size, differences in material composition, differences in flow properties, a single fluorescent marker or, preferably, a fluorescent label identifier." A fluorescent label identifier is defined on page 4 as "a coding label attached to a bead or group of beads either by adding ratios of fluorophore and a non-fluorophore or by adding multiple, preferably two, fluorophores in varying ratios."

Significantly, the main thrust of Yamashita is the use of a *group* of similarly tagged beads to encode each choice of synthon (or chemical group) in a step of a sequential synthesis of a combinatorial library member. The beads are peripherally tagged with a fluorescent label identifier such that:

1. all of the beads in a given group will have the same fluorescence intensity and different groups will have intensities that differ from any other group by a factor of at least two, preferably three or more;

2. multiple, preferably two, different fluorescent tags are used in varying ratios, such that all of the beads in a given group will have the same combination of fluorescent tags in the same ratio and different groups will have:
   (a) the same fluorescent tags but ratios that differ from any other group;
   (b) a different set of fluorescent tags in a specified ratio; or
   (c) a combination of (a) and (b) (see page 17, last paragraph).

The *groups* of beads disclosed by Yamashita require the beads to be similarly tagged for encoding a single synthetic step in each library of a series of combinatorial libraries (see page 5, line 12 to page 15, line 33 and page 17, lines 16 to 21), wherein the encoded step of any library is different from the other libraries of the series (see page 5, lines 9-11) and wherein the beads of each library are exposed to the same synthetic steps. Prior to encoding a synthetic step in each library, a sorting procedure is performed in which a group of similarly tagged beads is sorted into a number of containers corresponding to the number of different choices of building block or "synthon" for the synthetic step. The combinatorial libraries thus prepared will contain tagged beads that identify the reaction sequence of a single synthetic step only (see page 15, lines 29-32).

In contrast, the Examiner will note that the plurality of carriers recited in the pending claims includes a population of detectably distinct carriers, each having a code that distinctly identifies a respective carrier from other carriers before, during and after compound synthesis. Yamashita teaches populations of similarly tagged beads, which by definition are not detectably distinct.

Additionally, when used in methods of synthesizing and deconvoluting a combinatorial library, the plurality of carriers, which includes the detectably distinct population of carriers, is not sorted into reaction vessels according to any common tagging aspect, as taught by Yamashita. Instead, the codes of the plurality of carriers are simply recorded to track the movement of individual detectably distinct carriers (*e.g.*, using a flow cytometer) through the series of synthesis steps from which the combinatorial library is synthesized. In this manner, each synthon in a respective synthetic step is matched to a specific detectably distinct carrier. By contrast, Yamashita matches each synthon in a respective reaction step to a group of beads having a common code and do not disclose any bead that is individually tracked during

combinatorial library synthesis.

The Examiner cites the disclosure of Jai-ping *et al*. in support of the contention that Yamashita's use of flow cytometry would inherently disclose light scattering and fluorescence (Office communication page 6). The Examiner points to Jai-ping's teaching that flow cytometry can be used for multi-parameter sorting, based on, *e.g.*, fluorescence and scattering as a basis for this assertion. (Office communication page 5). Applicants respectfully disagree with the Examiner's conclusions, and respectfully point out that the fact that flow cytometry *could* use light scattering as a basis for bead differentiation does not mean that all beads analyzed by flow cytometry can be differentiated based on light scattering.

As noted above, "features" of the claimed carriers must define the code such that the code distinctively identifies its respective carrier. Furthermore, the features of the carriers are intrinsic to the carrier. For the reasons discussed above, Applicants maintain that Yamashita does not teach or disclose a carrier having a light scattering "feature" that defines the code that distinctively identifies its respective carrier. The capabilities of flow cytometry with respect to multiparameter analysis, even if the capabilities comprise detection of scattering, do confer on the Yamashita beads a feature that is otherwise absent. Neither Yamashita nor Jai-ping teach or suggest that the beads of Yamashita are, or could be distinctively identified based on a light scattering property, as required by the instant claims. As such, Applicants maintain that Yamashita, even if considered in view of Jai-ping, does not teach or suggest the light scattering "feature" of the instant claims. As such, Yamashita fails to teach each of the elements of the instant claims and Applicants respectfully submit that the claims are not anticipated by Yamashita and respectfully request that these rejections be withdrawn.

III. Claims 15 and 18-21 stand rejected under 35 U.S.C. 102(e) as allegedly being anticipated by Seul et al (USP 7083914). In particular, the Examiner points to column 5, line 26 through column 6 line 56 and asserts that the color codes of Seul encompass the light emitting features of the instant claims. Applicants respectfully disagree.

Embodiments of the instant claims recite "A plurality of carriers . . . comprising a population of detectably distinct carriers . . . each carrier having a code which distinctively identifies a respective carrier **before, during and after a combinatorial synthesis** from other

carriers." In contrast to the carriers of the instant claims, the particles of Seul are tagged during combinatorial synthesis. See, *e.g.*, Seul at column 6, lines 47-54, which states:

> Implementation of Color Codes
>
> The color coding strategy of the present invention provides a method to place a set of fluorophores---or, more generally, chromophores-on each bead so as to uniquely encode the chemical identity of the compound on that bead. Specifically, **during each coupling step in the course of DCR combinatorial synthesis, one or more fluorophores are attached to each bead**.

(column 6, lines 47-54, emphasis added)

Seul does not teach or suggest use of the beads that are coded prior to combinatorial synthesis. Rather, the Seul teaches that, for combinatorial synthesis application, coding occurs *during* synthesis. While not acquiescing that Seul teaches the other elements of Claim 15, Applicants respectfully point out that the beads of Seul do not comprise codes that distinctively identify the carrier *before, during, and after a combinatorial synthesis*. For these reasons, Applicants respectfully submit that the claims are not anticipated by Seul and respectfully request that these rejections be withdrawn.

IV. Claims 15, 18-29, 63 and 65-66 stand rejected under 35 U.S.C. 102(e) as allegedly being anticipated by Kauvar et al (USP 6642062) (as evidenced by Tao Jai-ping *et al.* (Chinese Journal of Physical Medicine (Vol. 17(3), September 1995, p 168-171) and by applicants' disclosure of known prior art. Kauvar discloses using combinations of dyes, particularly fluorescent dyes, to generate multihued labels.

Kauver does not teach the use of the multihued beads as a carrier for combinatorial synthesis. Rather, for combinatorial library screening, Kauver teaches that the addition of color generating moieties..."can be carried out in conjuction with the synthesis of the library members"...' (Col 9, line 35). That is, Kauver teaches encoding the particles during the combinatorial synthesis. Applicants note that, even though Kauver suggests coding during combinatorial synthesis, there is no disclosure of how to accomplish such coding.

As discussed above, the instant claims recite "A plurality of carriers . . . comprising a population of detectably distinct carriers . . . each carrier having a code which distinctively

identifies a respective carrier **before, during and after a combinatorial synthesis** from other carriers..

Kauver does not teach or suggest Kauver *et al.* do not teach or suggest a plurality of carriers comprising a population of detectably distinct carriers . . . each carrier having a code which distinctively identifies a respective carrier **before, during and after a combinatorial synthesis** from other carriers. The teachings of Jai-ping are discussed above. As previously noted, the capabilities of multiparameter flow cytometry as disclosed by Jai-ping do not confer features on the beads of Kauver. Neither Kauver nor Jai-ping teach or suggest that the beads of Kauvewr are, or could be distinctively identified before, during and after combinatorial synthesis, as required by the instant claims. As such, Applicants submit that Kauver, even if considered in view of Jai-ping, does not teach or suggest the elements of Claims 15, 18-29, 63 and 65-66, and therefore does not anticipate these claims. Applicants therefore respectfully request that these rejections be withdrawn.

The Claims Are Not Obvious

As the Board of Patent Appeal and Interferences has confirmed, a proper obviousness determination requires that an Examiner make "a searching comparison of the claimed invention – *including all its limitations* – with the teaching of the prior art." *See In re Wada and Murphy*, Appeal 2007-3733, *citing In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995) (emphasis in original). Further, the necessary presence of all claim features is axiomatic, since the Supreme Court has long held that obviousness is a question of law based on underlying factual inquiries, including … ascertaining the differences between *the claimed invention* and the prior art. *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966) (emphasis added). Indeed, Section 904 of the MPEP instructs Examiners to conduct an art search that covers "the invention *as described and claimed*." (emphasis added). Lastly, Applicants respectfully direct attention to MPEP § 2143, the instructions of which buttress the conclusion that obviousness requires at least a suggestion of all of the features of a claim, since the Supreme Court in *KSR Int'l v. Teleflex Inc.* stated that "there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (*quoting In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006).

In sum, it remains well-settled law that obviousness requires at least a suggestion of all of the features in a claim. *See In re Wada and Murphy*, *citing CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) and *In re Royka*, 490 F.2d 981, 985 (CCPA 1974)).

V. Claims 15, 18-29, 63 and 65-66 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over anyone of the cited references above e.g., Egner et al, Kauvar, Yamashita or Seul (hereinafter the primary references) in view of either Kris et al (USP 6238869) or Kimura et al (USP 6228480). Applicants respectfully disagree. The teachings of Egner, Kauver, Yamashita, and Seul are discussed above. For the reasons recited above, Applicants submit that none of these references teach or suggest each of the elements of the instant claims. Kris discloses the properties of certain solids. Kimura discloses the properties of certain adhesive layers and solids. Kris and Kimura fail to cure the deficiencies of Egner, Yamashita ,Seul and, Kauvar. Applicants therefore request that these rejections be withdrawn.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that all grounds for rejection have been addressed and Applicants' claims should be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourages the Examiner to call the undersigned collect at (608) 662-1277.

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